

WHAT IS CLAIMED:

1. A method of increasing the level of expression of a recombinant protein *in vivo* in cells of an individual, wherein the protein is expressed from an expression vector which has been introduced into the cells, which method comprises administering to the individual an active site-specific chaperone of the protein.

2. The method of claim 1, wherein the vector is a viral vector.

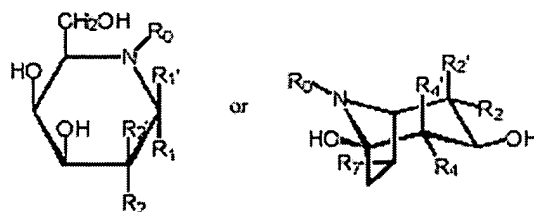
3. The method of claim 2, wherein the viral vector is an adenoviral vector.

4. The method of claim 1, wherein the protein is an enzyme and the active site-specific chaperone is a reversible competitive inhibitor of the enzyme.

5. The method of claim 4, wherein the enzyme is α -galactosidase A.

6. The method of claim 4, wherein the enzyme is β -glucocerebrosidase..

7. The method of claim 5, wherein the reversible competitive inhibitor is a compound of the following formula:



wherein R₀ represents H or a C₁-C₁₂ alkyl chain;

R₁ and R₁' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group;

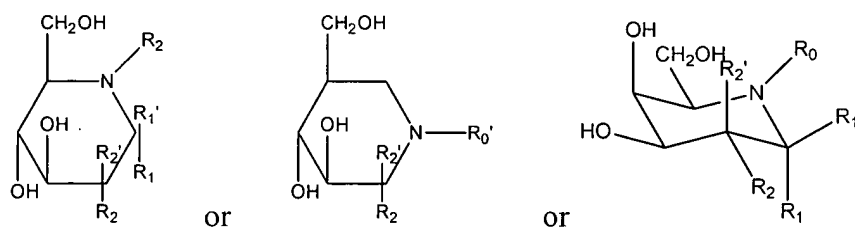
R₂ and R₂' independently represent H, OH or a C₁-C₁₂ alkyl group

R_4 and R_4' independently represent H, OH; and
 R_7 represents H or OH.

8. The method of claim 7, wherein the reversible competitive inhibitor is a compound selected from the group consisting of 1-deoxygalactonojirimycin, α -*allo*-homonojirimycin, α -*galacto*-homonojirimycin, α -1-C-butyl-deoxynojirimycin, calystegine A₃, calystegine B₂, N-methyl-calystegine A₃, and N-methyl-calystegine B₂.

9. The method of claim 7, wherein the reversible competitive inhibitor is 1-deoxygalactonojirimycin.

10. The method of claim 6, wherein the reversible competitive inhibitor is a compound of the following formula:



wherein R_0 represents H or a C_1 - C_{12} alkyl chain;

R_0' represents H, a straight chain or branched saturated carbon chain containing 1-12 carbon atoms, optionally substituted with a phenyl, hydroxyl or cyclohexyl group;

R_1 and R_1' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group; and

R_2 and R_2' independently represent H, OH or a C_1 - C_{12} alkyl group.

11. The method of claim 10, wherein the reversible competitive inhibitor is a compound selected from the group consisting of isofagomine, N-dodecyl-isofagomine, N-nonyl-isofagomine, N-dodecyl-deoxynojirimycin, calystegine A₃, calystegine B₂, calystegine B₃ and calystegine C₁.

12. The method of claim 11, wherein the reversible competitive inhibitor is isofagomine.

13. The method of claim 11, wherein the reversible competitive inhibitor is N-dodecyl-isofagomine.

5

14. A method of increasing the level of expression of a recombinant protein *in vivo*, wherein the protein is expressed by host cells comprising an expression vector encoding the protein, which method comprises co-administering to the individual the host cells and an effective amount of an active-site specific chaperone of the protein.

10

15. The method of claim 14, wherein the vector is a viral vector.

16. The method of claim 15, wherein the viral vector is an adenoviral vector.

15

17. The method of claim 15, wherein the host cells are human primary cells and the individual is a human.

18. The method of claim 17, wherein the human cells are mesenchymal stem cells.

20

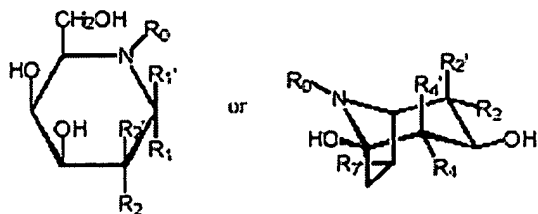
19. The method of claim 14, wherein the protein is an enzyme.

20. The method of claim 19 wherein the enzyme is α -galactosidase A.

21. The method of claim 19, wherein the enzyme is β -glucocerebrosidase.

25

22. The method of claim 20, wherein the reversible competitive inhibitor is a compound of the following formula:



wherein R_0 represents H or a C_1 - C_{12} alkyl chain;

R_1 and R_1' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group;

5 R_2 and R_2' independently represent H, OH or a C_1 - C_{12} alkyl group

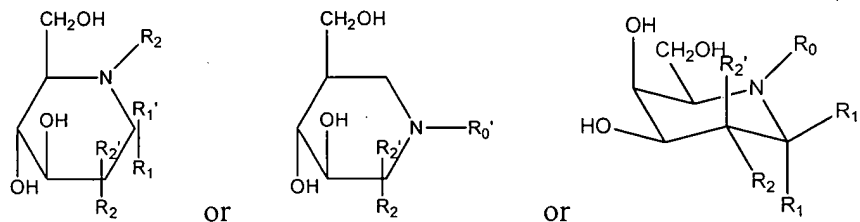
R_4 and R_4' independently represent H, OH; and

R_7 represents H or OH.

23. The method of claim 22, wherein the reversible competitive inhibitor is a compound
10 selected from the group consisting of 1-deoxygalactonojirimycin, α -*allo*-homonojirimycin, α -*galacto*-homonojirimycin, α -1-C-butyl-deoxynojirimycin, calystegine A_3 , calystegine B_2 , N-methyl-calystegine A_3 , and N-methyl-calystegine B_2 .

24. The method of claim 23, wherein the reversible competitive inhibitor is 1-
15 deoxygalactonojirimycin.

25. The method of claim 21, wherein the reversible competitive inhibitor is a compound of the following formula:



wherein R_0 represents H or a C_1 - C_{12} alkyl chain;

R_0' represents H, a straight chain or branched saturated carbon chain containing 1-12 carbon atoms, optionally substituted with a phenyl, hydroxyl or cyclohexyl group;

R_1 and R_1' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group; and

R_2 and R_2' independently represent H, OH or a C_1 - C_{12} alkyl group.

5 26. The method of claim 25, wherein the reversible competitive inhibitor is a compound selected from the group consisting of isofagomine, N-dodecyl-isofagomine, N-nonyl-isofagomine, N-dodecyl-deoxynojirimycin, calystegine A_3 , calystegine B_2 , calystegine B_3 and calystegine C_1 .

10 27. The method of claim 26, wherein the reversible competitive inhibitor is isofagomine.

 28. The method of claim 26, wherein the reversible competitive inhibitor is N-dodecyl-isofagomine.

15 29. A method of treating an individual having a disorder requiring gene therapy, comprising administering to the individual a composition comprising a therapeutic vector encoding a protein and an active site-specific chaperone for the protein.

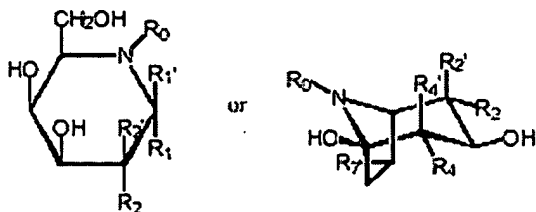
 30. The method of claim 29, wherein the protein is an enzyme and the active site-specific
20 chaperone is an inhibitor of the enzyme.

 31. The method of claim 30 wherein the enzyme is associated with a lysosomal storage disorder.

25 32. The method of claim 31, wherein the enzyme is α -galactosidase A.

 33. The method of claim 31, wherein the enzyme is β -glucocerebrosidase.

 34. The method of claim 32, wherein the reversible competitive inhibitor is a compound
30 of the following formula:



wherein R_0 represents H or a C_1 - C_{12} alkyl chain;

R_1 and R_1' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group;

R_2 and R_2' independently represent H, OH or a C_1 - C_{12} alkyl group

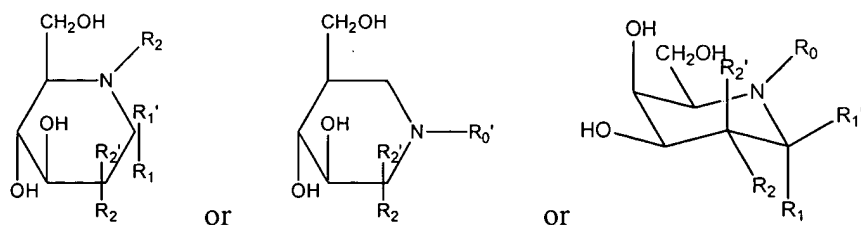
R_4 and R_4' independently represent H, OH; and

R_7 represents H or OH.

35. The method of claim 34, wherein the reversible competitive inhibitor is a compound selected from the group consisting of 1-deoxygalactonojirimycin, α -*allo*-homonojirimycin, α -*galacto*-homonojirimycin, α -1-C-butyl-deoxynojirimycin, calystegine A₃, calystegine B₂, N-methyl-calystegine A₃, and N-methyl-calystegine B₂.

36. The method of claim 35, wherein the reversible competitive inhibitor is 1-deoxygalactonojirimycin.

37. The method of claim 33, wherein the reversible competitive inhibitor is a compound of the following formula:



wherein R_0 represents H or a C_1 - C_{12} alkyl chain;

R₀' represents H, a straight chain or branched saturated carbon chain containing 1-12 carbon atoms, optionally substituted with a phenyl, hydroxyl or cyclohexyl group;

R₁ and R₁' independently represent H, OH, a 1-4 carbon alkyl, alkoxy or hydroxyalkyl group; and

5 R₂ and R₂' independently represent H, OH or a C₁-C₁₂ alkyl group.

38. The method of claim 37, wherein the reversible competitive inhibitor is a compound selected from the group consisting of isofagomine, N-dodecyl-isofagomine, N-nonyl-isofagomine, N-dodecyl-deoxynojirimycin, calystegine A₃, calystegine B₂, calystegine B₃ and
10 calystegine C₁.

39. The method of claim 38, wherein the reversible competitive inhibitor is isofagomine.

40. The method of claim 38, wherein the reversible competitive inhibitor is N-dodecyl-
15 isofagomine.